IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GILEAD SCIENCES, INC., GILEAD PHARMASSET LLC and GILEAD SCIENCES LIMITED,

Plaintiff, Defendants, Counterclaim Plaintiffs and Third Party Plaintiffs,

v.

ABBVIE, INC., and

Defendant, Plaintiff, Counterclaim Defendant, and Counterclaim Plaintiff.

ABBVIE IRELAND UNLIMITED COMPANY,

Counterclaim Plaintiff.

C.A. No. 13-2034-GMS

(Consolidated with C.A. Nos. 14-209, 14-379)

DECLARATION OF DR. NEZAM AFDHAL
REGARDING CLAIM CONSTRUCTION FOR
U.S. PATENT NOS. 8,466,159, 8,492,386, 8,680,106, 8,685,984, & 8,809,265

1. I have been retained by Gilead Sciences, Inc., Gilead Pharmasset LLC, and Gilead Sciences Limited (collectively, "Gilead") in the patent infringement lawsuits referenced above as a technical expert on the subject of Hepatitis C ("HCV") and treatment for HCV. A copy of my current and complete curriculum vitae is attached to this Declaration as Exhibit A.

2. I understand that the parties in this case will be asking the Court to define certain terms contained in the claims of United States Patent Nos. 8,466,159, 8,492,386, 8,680,106, 8,685,984, and 8,809,265 in a process I understand is referred to as "claim construction." I will

refer to these patents individually by their last three digits and to them collectively as the "patents-in-suit".

3. I have been asked by Gilead to provide an explanation, for the benefit of the Court, of how a physician treating patients with HCV as of approximately 2011 to 2012 would have understood certain aspects of the patents that relate to disputed claim terms. I have also been asked to explain how certain terms used in the patents-in-suit would be understood as of 2011 to 2012. This declaration contains those explanations.

4. I am prepared to testify before the Court about the explanations contained in this Declaration, if called upon to do so.

5. I am being compensated for the services I render in this case at an hourly rate of $650.00 per hour plus reasonable expenses. My compensation is in no way based on the outcome of this litigation. I have no vested interest, financial or otherwise, in the outcome of the current patent infringement litigation between these companies.

I. EDUCATION, PROFESSIONAL EXPERIENCE, AND QUALIFICATIONS

6. My education and experience is described more fully in the attached curriculum vitae (Exhibit A). I nonetheless highlight certain achievements here.

7. I have over 25 years of research experience in gastroenterology and hepatology, including the study and clinical investigation of HCV treatment, which is particularly relevant to the issues disclosed below.

8. I received a Bachelor of Medicine, Bachelor of Surgery degree from the Royal College of Surgeons in Ireland in 1981. After receiving my medical degree I completed postdoctoral training, including fellowships in gastroenterology at St. Vincent's Hospital, University College Dublin, Dublin, Ireland and Boston University, Boston, MA.

9. After completing my postdoctoral training, I became an Assistant Professor of medicine at Boston University from 1989-1994 and was subsequently promoted to Associate Professor from 1994-2000. From 2000-2012, I was an Associate Professor of medicine at Harvard Medical School, Cambridge, MA. From 2012 to the present I have been a Professor of medicine there.

10. Coinciding with my teaching positions, I held various appointments at hospitals and affiliated institutions. Notably, from 1993-2000, I was Section Chief of Hepatology/Medicine at Boston Medical Center, Boston, MA. From 2000-2014, I was Division Chief of Hepatology at Beth Israel Deaconess Medical Center in Boston, MA. As of 2015 to date, I am the Division Senior Physician in Hepatology at Beth Israel Deaconess Medical Center.

11. Over the course of my career, I received numerous honors and prizes among which include: the Charles Trey Research award (1989) by the American Liver Foundation, the Award of Excellence in Clinical Care (1995) by the American Liver Foundation, named Fellow (1995) at Royal College of Physicians of Ireland, named Fellow (2001) at the American College of Gastroenterology, and named Fellow (2014) at the American Association for the Study of Liver Diseases (AASLD).

12. I actively participate in a number of professional societies including the Academy of Medicine of Ireland, Irish Society of Gastroenterology, Gastroenterology Research Group, the American Gastroenterology Association (where I currently serve as Councilor, Liver Biliary Section), AASLD (where I currently serve as Chair of the Abstracts Committees, Hepatitis), British Society of Gastroenterology, European Association for the Study of Liver Diseases, and Liver Institute for Education and Research.

13. I currently serve as the U.S. Senior Editor for the Journal of Viral Hepatitis. Previously, I served on the editorial board of Gastroenterology, Physicians Home Page, Gastroenterology and Hepatology, Journal of Viral Hepatitis, and Clinical Gastroenterology and Hepatology. I also serve as an ad hoc reviewer for these journals, as well as the New England Journal of Medicine, Journal of Hepatology, American Journal of Gastroenterology, Liver Transplantation, Annals of Internal Medicine, Lancet, Nature, Gut, and Alimentary Pharmacology and Therapeutics.

14. I have authored or co-authored more than 160 scientific publications, 2 books, and numerous book chapters, non-print materials, and clinical communications.

15. As part of my work on this matter and in connection with this Declaration, I have reviewed portions of the materials listed in Exhibit B. Based on my education and experience, and my review of the materials listed in Exhibit B, I have formed certain opinions and made certain observations regarding how "a person of skill in the art," as I understand that term, would have understood certain terms in the claims of the patents-in-suit, explained in greater details in the sections to follow. I believe that my opinions and observations may assist the Court in its determination of the claim construction issues raised by the parties.

II. LEGAL PRINCIPLES

16. In expressing opinions on what I understand might be considered to be legal issues, I have applied the following legal standards conveyed to me by Gilead's counsel.

17. I understand from Gilead's counsel that terms in the patent claims must be read as they would have been understood by a "person of ordinary skill in the art" at the relevant time period. I have been advised by Gilead's counsel that the relevant time period is approximately 2011-2012.

18. I understand that a hypothetical person of ordinary skill in the art related to the patents-in-suit would include a person with a scientific degree, either Ph.D., Pharm.D., or M.D., who has at least 2-3 years of experience developing or researching antiviral treatment methods, such as treatment methods for HCV; or has 2-3 years of experience as a specialist in treating HCV (e.g., a hepatologist or gastroenterologist) and may have also assisted in developing or researching antiviral treatment methods. This person would additionally have at least some experience either developing, researching, or treating patients with treatments that include Direct Acting Antivirals. This person may also work in collaboration with other individuals who have experience developing or researching antiviral treatments and treatment methods, such as pharmacologists, chemists and/or virologists, running clinical trials related to such treatments, and/or treating patients using such treatments. Under this definition, I am at least a person of ordinary skill in the art, and was during the relevant time period, 2011-2012.

III. BACKGROUND - HEPATITIS C AND TRADITIONAL TREATMENT

19. HCV is a highly contagious group of viruses that is estimated to infect as many as 4 million people in the United States and 170 million worldwide. HCV is spread by contact with infected blood. In some patients HCV can cause serious liver damage, including cirrhosis, liver cancer, and liver failure. Treatment for hepatitis C includes liver transplantion, and HCV is currently the commonest cause for liver transplant in the U.S.

20. Until very recently, the “standard of care” used by health care professionals to treat chronic HCV infection was a combination of two drugs: (1) interferon, which is taken through a weekly injection, and (2) ribavirin, which is taken as a pill in divided doses daily based on weight. The “standard of care” treatment lasted up to 48 weeks, had relatively limited efficacy, and caused severe side effects and was poorly tolerated by many patients.

21. The approval of two direct acting anti-viral agents ("DAAs") called boceprevir and telaprevir in 2011 changed the standard of care for one type of hepatitis C, genotype 1, to allow for durations down to 24 weeks in some patients, but the treatment still required the use of interferon and ribavirin, with all their accompanying side effects. DAAs are compounds that interfere with specific steps in the HCV replication cycle through a direct interaction with the HCV genome.

22. In 2011, treatment for HCV with interferon-based therapies including telaprevir and boceprevir was predominantly used in patients with significant fibrosis or scarring because the risk benefit ratio did not favor treating patients with mild disease (no or minimal scarring).

23. Within the past few years, a number of companies have worked on developing DAAs for the treatment of HCV, working toward a treatment regimen that would allow for the elimination of interferon and ribavirin.

24. The FDA approved two Gilead DAA products in 2014—SOVALDI®, which contains the DAA sofosbuvir, and HARVONI®, which contains a combination of the DAAs sofosbuvir and ledipasvir. These products represent a major advance in HCV treatment. SOVALDI® in combination with ribavirin became the first approved interferon-free therapy for certain HCV patients, those with genotypes 2 and 3. HARVONI® is the first all-oral, interferon and ribavirin-free therapy that can also be used for HCV patients with genotype 1 disease, the most common genotype accounting for 70% of U.S. patients.

IV. THE TERM "TREATMENT FOR HCV" AS USED IN ABBVIE'S PATENTS

25. It is my opinion that a person of ordinary skill in the art would have understood the term "treatment for HCV," as used in the context of AbbVie's patents at issue here, to mean medical measures that are given to patient for the purpose of stopping or slowing the progression of HCV.

26. I understand from Gilead's counsel that the following claims are asserted in this case: claims 13-16 of U.S. Patent No. 8,466,159; claims 13-16 of U.S. Patent No. 8,492,386; claims 6-12 and 17-20 of U.S. Patent No. 8,680,106; claims 6-12 and 17-20 of U.S. Patent No. 8,685,984; and claims 1, 3, and 4 of U.S. Patent No. 8,809,265. I refer to those claims below as the "asserted claims."

A. "Treatment for HCV" has a Well Understood Meaning in the Field

27. "Treatment for HCV" has a well understood meaning to physicians in the field: it refers to the medical measures given to a patient for the purpose of stopping or slowing the progression of HCV. "Treatment for HCV" does not imply that the treatment is effective, nor does it imply any particular measure of efficacy.

28. In my experience, the ordinary meaning of "treatment for HCV" as used by those who practice in this field does not relate to or require achievement of any particular result.

29. Indeed, there were several clinical trials running in approximately the 2011 to 2012 timeframe where the treatment regimen being investigated was found to be unsuccessful. But those regimens were still referred to by those in the field as "treatments for HCV." For example, it was announced in December 2010 that two treatment arms in the clinical trial investigating VX-222 and telaprevir in treatment-naïve patients with genotype 1 HCV were being discontinued because of unacceptable rates of viral breakthrough. The discontinued arms included VX-222 with telaprevir for 12 weeks of treatment without interferon or ribavirin.

Although these arms were ultimately not successful, they were still "treatments for HCV," as that phrase is used by those skilled in the art.

30. Treatments for HCV also included treatments that were designed to slow down disease progression and scarring without necessarily affecting the HCV virus levels and included protective agents such as silymarin for liver disease.

31. The phrase "treatment for HCV" does not require achievement of a certain level of efficacy. In particular, it does not require "significant efficacy, as may be measured by SVR," as I understand AbbVie has suggested. AbbVie's definition appears to focus on achieving SVR, but there were a number of treatments for HCV in the relevant timeframe that had nothing to do with attacking the virus. A treatment for HCV can also be directed to dealing with damage to the liver, inflammation, or other complications of the disease. For example, an NIH trial that ran shortly before the 2011 to 2012 timeframe looked at "treating" HCV by dealing with liver injury utilizing silymarin, as mentioned above.

32. Thus, any definition of "treatment for HCV" that focuses only on the viral level is not consistent with the understanding of those in the art at the time.

33. My understanding of the term "treatment for HCV" is also consistent with the known meaning of "treatment" in the medical world as defined in common medical dictionaries used in my practice and the practice of other clinicians. For example, *Dorland's Medical Dictionary* defines "treatment" as "the management and care of a patient for the purpose of combating disease or disorder." (*Dorland's Illustrated Medical Dictionary* 1957 (32d Edition 2012). Likewise, *Stedman's Medical Dictionary* broadly defines "treatment" as "[m]edical or surgical management of a patient." *Stedman's Medical Dictionary for the Health Professions and Nursing* 1712 (7th Edition 2012). Using these definitions I would also believe that a person

of ordinary skill would consider that treatment of HCV would also include treating the direct complications or consequences of the disease including liver failure and liver cancer, which are treated by medicines that do not attack the virus or by surgical procedures such as liver transplantation.

34. In my opinion, for the reasons set forth above, a person of ordinary skill in the art as of approximately 2011-2012 would have understood "treatment of HCV" to mean medical measures given to a patient for the purpose of stopping or slowing the progression of HCV.

B. The Specification of AbbVie's Patents Use "Treatment for HCV" Consistently with its Ordinary Meaning

35. I have reviewed AbbVie's patents at issue. They do not define the term "treatment for HCV."

36. As I read the specification of the patents-in-suit, "treatment for HCV" is described separately from the "efficacy" of treatment. For example, the term "treatment" is used to simply refer to giving a combination of direct acting antiviral (DAA) compounds to a patient with HCV. As one example of this, the specification states that "the present technology features a combination of PSI-7977 and GS-5885 for use in treating HCV infection. The treatment comprises administering the DAA combination to a subject infected with HCV." ('159 patent at 16:47-17:52; *see also* '159 patent at 10:52-11:18 ("The treatment comprises administering PSI-7977 or the DAA combination to a subject infected with HCV."); *id.* at 10:15-42; 11:19-52.) Nothing about these statements suggests to me that the DAA combinations given to a patient must be effective, much less that they must achieve "significant' efficacy, in order to be considered "treatment for HCV." Rather, they support the ordinary meaning of "treatment for HCV," which is that the DAA combinations are given to patients for the purpose of stopping or slowing the progression of HCV.

37. After broadly describing the methods for treating HCV as "administering at least two direct acting antiviral agents (DAAs) and ribavirin to a patient for a duration of no more than 12 weeks," the specification often states that "preferably," the DAA combinations "are administered in amounts effective to provide a sustained virological response (SVR) or achieve another desired measure of effectiveness in a subject." (*See* '159 patent at 1:40-50.) A person of skill in the art reading these sate would not understand this to mean that the methods for treatment of HCV ***require*** efficacy, only that it is preferred as the goal of the treatment.

38. The specification also states that "[v]arious measures may be used to express the effectiveness of the present measures of HCV treatment," including rapid virological response (RVR), early virological response (EVR), complete early virological response (cEVR), extended rapid virological response (eRVR), end of therapy (EOT), and sustained virological response (SVR). ('159 patent at 27:38-67.) Once again, this would show a person skilled in the art that "treatment" is being used separately from the effectiveness of that treatment. When the patent specification discusses measures of efficacy, it refers specifically to those measures. The asserted claims of AbbVie's patents do not refer to efficacy or any measures of efficacy.

39. In my experience, terms such as RVR, EVR, cEVR, eEVR, EOT, and SVR are all useful measures to express the effectiveness of a treatment given to a patient with HCV. The term "treatment" by itself does not imply the use of any particular measure. I disagree with AbbVie's definition of "treatment for HCV" to the extent it focuses only on SVR as a measure of effectiveness. In practice, other measurements—shorter term measurements like RVR and EVR, for example—are also used by clinicians to evaluate the effectiveness of a treatment given to a patient with HCV.

40. In my opinion, a person of ordinary skill in the art would have understood "treatment for HCV" in the context of the claims and the specification of AbbVie's patents at issue to be consistent with its ordinary meaning, that is, given for the purpose of stopping or slowing the progression of HCV.

V. CONCLUSION

41. This Declaration is based on my study of the information available to me at the time of its writing. My review and consideration of the patents-in-suit, their claims, and the other materials discussed in this Declaration are ongoing. As my analysis continues, I may identify additional evidence supporting the opinions that I have summarized in this Declaration. I reserve the opportunity to update, supplement, or amend this Declaration in view of further analysis or additional information that might be obtained or become available at a later time or to address new or different positions taken by AbbVie.

Dated: 8/4/15

Dr. Nezam Afdhal